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**REMARKS**

Claims 57-60 and 76-78 are pending in the subject application. Applicants have not added, canceled or amended any claims. Accordingly, claims 57-60 and 76-78 are still pending and under examination in the subject application.

**Rejection under 35 U.S.C. 103(a)**

The Examiner rejected claims 57-60 and 76-78 under 35 U.S.C. §103(a) as allegedly obvious over Hori, et al. ("Hori"), in view of Miki, et al. ("Miki") and Parkkinen, et al. ("Parkkinen").

Specifically, the Examiner alleges that the RAGE-amphoterin relationship and the role of amphoterin in tumor spreading are known in the art. Therefore, the Examiner alleges that it would have been obvious to one skilled in the art that inhibiting the RAGE-amphoterin interaction would necessarily inhibit tumor spreading. The Examiner further alleges that applicants have not provided evidence that there exists a compensatory or collateral pathway directly linked or associated with RAGE-amphoterin interaction. According to the Examiner, the Walker, et al. reference ("Walker") previously submitted by applicants in the April 3, 2006 Communication only teaches the general unpredictability associated with interpreting the effects of certain cellular pathways and further indicates that in the absence of certain protein targets, a compensatory or

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collateral pathway may exist.

In response to the Examiner's rejection, applicants respectfully traverse.

Applicants maintain that the Examiner has misinterpreted applicants' rationale for submitting Walker in connection with the subject application.

Walker teaches against the subject invention even when taken together with the cited references which are discussed in the April 3, 2006 Communication. Specifically, applicants submitted Walker in order to show the general understanding in the art that collateral and/or compensatory pathways *do* exist, and the presence of such pathways can *mitigate or even negate* the downstream effects of inhibiting the binding of a receptor with a ligand.

It is not applicants' position that there actually exists a compensatory or collateral cellular pathway linked to the RAGE-amphoterin relationship. In fact, evidence of such pathway, which the Examiner seems to demand, would be wholly incompatible with applicants' experimental findings and thus cannot be thought to exist.

Rather, applicants' position, as supported by the teachings of Walker, is that *absent* applicants' experiments upon which the claimed invention is based, one skilled in the art could not have reasonably ruled out the existence of a compensatory and/or collateral pathway in connection with

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RAGE-amphoterin interaction. Likewise, one could not have reasonably ruled out the possibility that such a pathway could mitigate or even negate the cellular effects of inhibiting the binding between RAGE and amphoterin. Only after applicants' experiments was it shown that no such compensatory or collateral pathway exists in connection with RAGE-amphoterin interaction, and that inhibiting binding between RAGE and amphoterin does indeed inhibit tumor spreading.

Accordingly, applicants maintain that claims 57-60 and 76-78 satisfy the requirements of 35 U.S.C. §103(a).

#### **Summary**

In view of the above remarks, applicants maintain that the pending claims are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

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No fee is deemed necessary in connection with the filing of this Communication. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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10/2/06  
Date